REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. Status of the Claims

Claims 1-24 were pending and under active consideration in the subject application. With this submission: (1) claims 1-12 and 21-24 are currently amended, (2) claims 15-20 have been cancelled, and (3) claims 25-31 are newly added. Hence, upon entry of this paper, claims 1-14 and 21-31 will remain pending and under active consideration.

II. Claim Amendments

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

Claims 15-20 are requested to be cancelled. The cancellation of claims does not constitute acquiescence in the propriety of any rejection set forth by the Examiner. Applicants reserve the right to pursue the subject matter of the canceled claims in subsequent divisional applications.

Support for newly added claims 25-31 can be found throughout the specification.

Claims 22-24 have been amended. Support for these amendments can be found throughout the specification. Additionally, the Office conceded that the invention is "enabling for treating...viral infectious diseases." (Office Action, page 6). Applicants have simply revised the claims to reflect this statement.

Applicants submit that the foregoing amendments do not introduce new matter, thus entry thereof by the Examiner is respectfully requested.

III. Species Election

Applicants wish to thank the Examiner for recognizing that "[t]he elected species is not fairly taught in the prior art." (Office Action, page 3) Applicants also wish to thank the Examiner for expanding the search to other and/or general species encompassed by the claims.

IV. Claim Rejection Under 35 U.S.C. §112 second paragraph

Claims 1-12, 15, 17, and 18-21 are rejected under 35 U.S.C. §112 second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Office argues that "[t]he term 'prodrug' in the instant claim is not described, explained or defined in the instant specification." (Office Action, page 3)

Without acquiescing to the propriety of the rejection, Applicants have deleted the quoted phrase "prodrug" from the claims, which should render the objection moot. Applicants thus respectfully request withdrawal of the objection insofar as the amendments to claims 1-12 and 21 render the subject rejection moot. Additionally, claims 18-20 have been cancelled rendering the subject rejection moot to claims 18-20. As such, Applicants respectfully request the Examiner to withdraw the 35 U.S.C. §112 second paragraph rejection.

V. Claim Rejection Under 35 U.S.C. §112 first paragraph

Claims 1-12, 15, 17, and 18-21 are rejected under 35 U.S.C. §112 first paragraph as allegedly not providing enablement for the prodrug of the pharmaceutical composition. Although the Office admits that the specification is "enabling for the pharmaceutical composition," the Office argues that the specification "does not provide enablement for the prodrug of the said pharmaceutical composition." (Office Action, page 4)

Without acquiescing to the propriety of the rejection, Applicants have deleted the quoted phrase "prodrug" from the claims, which should render the objection moot. Applicants thus respectfully request withdrawal of the objection insofar as the amendments to claims 1-12 and 21 render the subject rejection moot. Additionally, claims 18-20 have been cancelled

rendering the subject rejection moot to claims 18-20. As such, Applicants respectfully request the Examiner to withdraw the 35 U.S.C. §112 first paragraph rejection.

VI. Claim Rejection Under 35 U.S.C. §112 first paragraph

Claims 1-14 and 21-24 are rejected under 35 U.S.C. §112 first paragraph as allegedly not providing enablement for a person of skill in the art to use the invention commensurate in scope with these claims. Although the Office admits that the specification is "enabling for treating [viral infectious diseases,]" the Office argues that the specification "does not reasonably provide enablement for preventing viral infectious diseases." (emphasis added) (Office Action, page 6)

Without acquiescing to the propriety of the rejection, Applicants have deleted the quoted phrase "preventing" from the claims, which should render the objection moot. Applicants thus respectfully request withdrawal of the objection insofar as the amendments to claims 1 and 22 render the subject rejection moot, thus rendering the rejections of dependent claims 2-14 and 23-24 moot.

Claim 21 is not directed towards a method of preventing a disease, but only to the pharmaceutical composition itself; as such, applicants believe this rejection should not apply to claim 21.

For at least these reasons, Applicants respectfully request the Examiner to withdraw the 35 U.S.C. §112 first paragraph rejection.

VII. Claim Rejection Under 35 U.S.C. §103

Claims 15-24 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Esumi et al. ("Esumi"). The Office admits that Esumi "does not teach the virdiofungin A for the treatment of viral infections." (Office Action, page 14) However, the Office alleges that Esumi teaches "a core chemical moiety which makes formula (I) of claim 15 and 21 obvious in view of the claimed invention." (Office Action, page 14).

Without acquiescing to the propriety of the rejection, Applicants have cancelled claims 15-20, which should render the rejection moot. Additionally, claims 22-24 depend

indirectly or directly from claim 21, as such, applicants believe this amendment should render the rejection moot. Applicants thus respectfully request withdrawal of the objection insofar as the cancellation of claims 15-20 renders the subject rejection moot.

Claim 21 now depends from newly added claim 25. Applicants submit that Esumi does not render independent claims 25 and 31 or dependent claims 21-24 and 26-30 obvious for the reasons below.

A. Current Obviousness Standard

The Supreme Court recently reaffirmed the Graham factors for determining obviousness in *KSR Int'l Co. v. Teleflex Inc.* (No. 04-1350) (U.S., April 30, 2007). The Graham factors, as outlined by the Supreme Court in *Graham et al. v. John Deere Co. of Kansas City et al.*, 383 U.S. 1 (1966), are: 1) determining the scope and contents of the prior art; 2) ascertaining the differences between the claimed invention and the prior art; 3) resolving the level of ordinary skill in the pertinent art; and 4) evaluating evidence of secondary consideration. The Supreme Court recognized that a showing of "teaching, suggestion, or motivation" to combine the prior art to meet the claimed subject matter could provide a helpful insight in determining whether the claimed subject matter is obvious under 35 U.S.C. § 103(a), and held that the proper inquiry for determining obviousness is whether the improvement is more than the predictable use of prior art elements according to their established functions. The Court noted that it is "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements" in the manner claimed, and specifically stated:

> Often, it will be necessary . . . to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was ***an apparent reason to combine the known elements in the fashion claimed*** by the patent at issue. To facilitate review, this analysis should be made explicit.

KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 418 (2007) (emphasis added). As discussed below, the cited art cannot render the claimed invention obvious.

B. Esumi Does Not Teach the Compound of Claim 25

The compound of formula (I) of the subject application has a phenyl group which is substituted with alkynyloxy in the "group A" position (such as compound 21). In contrast, viridiofungin A, which is disclosed by Esumi, has a p-hydroxy-phenyl in the "group A" position.

The Examiner is reminded that "[t]he mere fact that references *can* be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art." M.P.E.P § 2143.01(III) citing *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1396 (2007) (emphasis in MPEP). Indeed, in order to properly establish a *prima facie* case for obviousness, "at least some degree of predictability is *required*." M.P.E.P. § 2143.02(II) (emphasis added).

None of the prior art, either alone or in combination, teaches or suggests all of the elements in the claims. As explained above, Esumi does not teach the alkynyloxy in the group A position. Additionally, one of skill in the art would not have easily conceived of substituting an alkynyloxy for a p-hydroxy-phenyl group. Furthermore, the Office has not given a reason for one of skill in the art to substitute an alkynyloxy group for the p-hydroxy-phenyl group of viridiofungin A. As such, applicants request reconsideration and withdrawal of the rejection.

C. No Expectation of Success

The M.P.E.P. states that "[t]he mere fact that references *can* be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art." M.P.E.P § 2143.01(III) citing *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1396 (2007) (emphasis in MPEP). Indeed, in order to properly establish a *prima facie* case for obviousness, "at least some degree of predictability is *required*." M.P.E.P. § 2143.02(II) (emphasis added).

Accordingly, it is difficult to predict the effect of the invention from the chemical structure. Even a person skilled in the art could not predict whether a compound having a structure defined by formula (I) in new claim 25 is useful for a medicament. Specifically, no

reference has described or suggested an anti-viral activity associated with the compound of formula (I).

Further, one of skill in the art would recognize that an alkynyloxyphenyl in "group A" in place of a hydroxyphenyl group would generate unpredictable results. This is because these two groups differ dramatically in both hydrophilicity and lipophilicity.

D. Esumi Does Not Teach Treatment of Viral Infections

The Office concedes that "Esumi et al. does not teach the viridiofungin A for the treatment of viral infections." (Office Action, page 14) Applicants have amended claims 22-24 to make clear that the method of treating viral infectious is claimed. Therefore applicants submit that the 35 U.S.C. §103a rejections of claims 22, 23, and 24 should no longer apply.

Applicants have shown that a phenyl group substituted with –OX (alkynyloxy) in the "group A" position generates a compound that has a therapeutic activity on viral infectious diseases such as HCV infection. In contrast, Esumi discloses a p-hydroxy-phenyl group in the "group A" position. Esumi discloses that viridiofungin A has an inhibitory activity only against squalene synthase and sphingolipid synthesis. However, as the Examiner correctly notes, there is no description or suggestion regarding the activities on viral infectious diseases.

Further, it cannot be expected that a compound having a phenyl group which is substituted with alkynyloxy would have a therapeutic activity on viral infectious diseases such as HCV infection. Specifically, as noted above, Esumi only describes inhibitory activities against squalene synthase and sphingolipid synthesis, which does not apply to viral infections. For at least these reasons, applicants respectfully request reconsideration and withdrawal of the rejection.

E. The Compound of Claim 25 Yields Unexpected Results

Evidence of unexpected results must be weighed against evidence supporting prima facie obviousness in making a final determination of the obviousness of the claimed

invention. *In re May*, 574 F.2d 1082, 197 USPQ 601 (CCPA178) (See also MPEP 716.02(c)).

Applicants have shown that a compound that has an alkynyloxyphenyl group (such as compound 21) has a much higher inhibitory activity as compared with Viridiofungin A. Specifically, compound 21 has the IC50 value of 0.001 which is much lower than that of Viridiofungin A (corresponding to compound 9) which has an IC50 value of 0.020. (See table on page 74 and 75) Therefore, inventors have shown that the claimed invention unexpectedly has a relatively lower cytotoxic effect.

For at least these reasons, Applicants respectfully request the Examiner to withdraw the 35 U.S.C. §103 rejection.

CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date July 9, 2009

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